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Association of immature granulocytes (IG) with prognosis in severe COVID-19 patients

İmmature granulocytes and COVID-19

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Abstract

Aim: Recent research have shown that immature granulocytes (IG) can be utilized to predict severe infection, inflammation, and sepsis. As a result, the ability of IG levels to predict the severity of severe COVID-19 and its association with prognosis were studied in our study.

Material and Mthods: A total of 317 patients diagnosed with severe COVID-19 in the emergency department were analyzed retrospectively. IGC and IG% levels were compared statistically between patient groups (survivors and non-survivors, those who received and did not get mechanical ventilation (MV) assistance, patients who required and did not require vasopressors, and hospital stays ≥10 and <10 days).

Results: When compared to patients who survived but did not get treatment, non-survivors who got MV and vasopressor support had substantially higher IGC and IG% values (for all p<0.001). Additionally, it was shown that the IG% of patients with hospital stays of ≥10 days was substantially greater than that of patients with hospital stays of <10 days (p<0.001). While the IG% cut-off value was >0.45, it reached 75.5% sensitivity, 81.9% specificity, 87.6% NPV and 66.4% PPV for predicting mortality (AUC:0.86, p<0.001).

Discussion: IG levels are a low-cost, easily accessible, and strong marker that may be used to predict mortality and prognosis in COVID-19 patients.

Keywords

Immature Granulocyte Count, COVID-19, Prognosis, Mortality

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Introduction

Coronavirus-19 (COVID-19), caused by SARS coronavirus 2 (SARS-CoV-2), is a fast-progressing disease that can result in major morbidity and mortality. The most important research priority in the COVID-19 pandemic is the identification of clinical and laboratory factors that predict prognosis. As a result, for risk categorization of these individuals, biomarkers that are easily accessible, affordable, and commonly employed are required [1]. Recently, it has been reported that hematological parameters and inflammatory indices have important predictive value for the prognosis of many diseases, including infections and COVID-19 [2].

Immature granulocytes (IG) in peripheral blood can form in response to infection, inflammation, or other bone marrow stimulation [3]. In recent studies, it has been determined that IG, which includes myelocytes, metamyelocytes, promyelocytes, is the precursor of neutrophils and can be monitored automatically in hemogram devices, can be utilized to predict severe infection, inflammation and sepsis [4]. Although the function of neutrophils in COVID-19 infection has been established [5], research examining IG levels and their association to prognosis in patients with severe COVID-19 appear to be few [6,7]. As a result, we studied the capacity of IG levels to predict the severity of severe COVID-19 and their relationship with prognosis in our study.

Material and Methods

Patients and study design

A total of 317 patients, respectively, who were hospitalized with a confirmed diagnosis of severe COVID-19 in the emergency department of a university hospital between May 1 and September 1, 2022, and met the inclusion criteria, were analyzed retrospectively. Patients older than 18 years of age, with a positive real-time reverse transcriptase polymerase-chain reaction (RT-PCR) result studied from a nasopharyngeal swab sample, with all clinical and laboratory information accessible from the hospital registry system and a confirmed diagnosis of severe/critical COVID-19 according to current guideline were included in the study (available at: https://covid19.saglik.gov.tr/TR-66301/covid-19-rehberi.html). Individuals under the age of 18, pregnant women, those with a history of acute/chronic hematological disease, liver or kidney failure, chronic alcohol or substance abuse, those receiving steroid therapy, cancers, those diagnosed with bacterial pneumonia/sepsis, autoimmune and immunosuppressive patients, those exposed to trauma, and patients whose records could not be reached in the electronic recording system were excluded from the study. By dividing neutrophil and platelet counts into lymphocytes, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated. All other parameters, particularly Immature granulocyte count (IGC) and Immature granulocyte percentage (IG%), were statistically compared between patients who survived and those who did not. Furthermore, IGC and IG% levels were compared between patients with and without mechanical ventilation (MV) and vasopressor support, hospital stays ≥10 days and <10 days. The Necmettin Erbakan University Faculty of Medicine Local Ethics Committee approved the study with the date 07/10/2022 and the number 2022/3999 (11425).

Data collection and laboratory tests

Age, gender, history, vital signs (fever, pulse, systolic blood pressure, saturation) at the time of admission to the emergency department of these patients and leukocytes (WBC), neutrophils, lymphocytes, monocytes, platelets (PLT), red blood cells distribution width (RDW%), IGC, IG%, hemoglobin (Hb), mean platelet volume (MPV), platelet distribution width (PDW), D-dimer, CRP, procalcitonin (PCT), and albumin values obtained from routine blood analysis, PCR result, thorax Spiral computed tomography (CT) report, whether they need mechanical ventilation (MV) (noninvasive/ invasive/ high-flow nasal cannula oxygen) or vasopressor support, total length of hospital stay and clinical outcomes (discharge/in-hospital death) were reached retrospectively from patient epicrisis. All data were collected through the hospital registry system by an emergency physician who had no knowledge of the study content and details. Complete blood count (CBC) was measured using Mindray auto hematology analyzer BC-6800 (Shenzhen, China). Biochemical parameters were obtained using Mindray chemistry analyzer BS-2000M device. Coronex COVID 19 QPCR (DS BIO and NANO Tech. Ltd., Ankara, Turkey) kit was used for the RT-PCR test.

Statistical analysis

Statistical analyzes of the data were performed using the SPSS 20.0 (SPSS Inc., Chicago, IL) package program. Normality analyzes of the data were performed using histograms and the Kolmogorov–Smirnov test. Since all linear variables were not normally distributed, median (25% - 75% quartiles) and all categorical variables were expressed as frequency (%). Differences between groups were expressed using the Mann–Whitney U test for linear variables and the chi-square test for categorical variables. Receiver operating characteristic (ROC) analysis was performed to evaluate the predictive power of laboratory parameters for in-hospital mortality. Laboratory parameters that achieved an area under the curve (AUC) value above 0.6 in the ROC analysis were categorized according to their optimum cut-off values using Youden's index (sensitivity + 1−specificity). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated according to the optimum cut-off values. Logistic regression analysis was performed to calculate the effect of important laboratory parameters on COVID-19 mortality. Once the parameters were categorized according to their optimal cut-off values, they were included in the regression analysis. First, univariate logistic regression analysis was performed. Parameters with a p-value less than 0.25 in the univariate analysis were included in the multivariate logistic regression analysis using the enter method. The Hosmer-Lemeshow test was performed to evaluate the model fit. A p-value of <0.05 was accepted for statistical significance.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

While 215 out of 317 patients survived, 102 patients did not survive. One hundred forty-two (44.8%) patients were male, with a mean age of 71 years (56-79) and a hospital stay of 9 days (5-14). Table 1 compares the demographic, clinical,

Table 1. Comparison of demographic, clinical and laboratory findings of survivor and non-survivor patients.

Variables		Nonsurvivors (n=102)	Survivors (n=215)	p value
Age		72 (58.75-78.25)	71 (54-79)	0.281*
Length of Hospital Stay (Day)		13 (8-20)	7 (5-11.25)	<0.001*
Gender	Male	56 (54.9%)	86 (40%)	0.013**
	Female	46 (45.1%)	129 (60%)	
Fever (ºC)		36.65 (36.08-37.8)	36.5 (36.2-37.1)	0.118*
Pulse (per minute)		96 (84.75-113.25)	74.5 (65-84)	<0.001*
SBP (mmHg)		95 (80-105.25)	125 (114-147.25)	<0.001*
Saturation (%)		78 (68-85)	89 (87-90)	<0.001*
IGC (10^9/L)		0.11 (0.04-0.33)	0.03 (0.01-0.63)	<0.001*
IG (%)		1.1 (0.48-2.2)	0.1 (0.004-0.3)	<0.001*
WBC (10^9/L)		8.48 (6.36-13.76)	7.63 (5.5-10.38)	0.025*
Neutrophil (10^9/L)		7.1 (5-12.07)	5.7 (3.98-8.55)	0.001*
Lymphocyte (10^9/L)		0.6 (0.33-0.9)	1.09 (0.6-1.6)	<0.001*
NLR		13.64 (6.93-26.88)	6.4 (2.86-12.81)	<0.001*
PLR		258.64 (148.52-476.54)	210.69 (140.25-387.5)	0.171*
Monocyte (%)		0.34 (0.2-0.67)	0.45 (0.3-0.6)	0.028*
RDW (%)		15.85 (14.1-18.15)	13.9 (13-15)	<0.001*
PDW (%)		16.3 (16.1-16.7)	16.1 (15.9-16.4)	<0.001*
Hb (g/dL)		11.45 (9.48-13.2)	12.95 (11.78-14)	<0.001*
PLT (10^9/L)		160 (110.5-231.5)	218 (177.75-276)	<0.001*
MPV (fL)		10.1 (9.18-11.1)	10 (9.3-10.9)	0.54*
D-Dimer (µg/L)		914 (398-2672.75)	610 (250-1079)	<0.001*
CRP (mg/L)		136.03 (70.41-206.62)	18 (6.5-54.5)	<0.001*
PCT (ng/ml)		0.68 (0.16-3.12)	0.06 (0.03-0.2)	<0.001*
Albumin (g/dL)		34.05 (29.33-37.63)	41.8 (38.08-44.83)	<0.001*
MV support		100 (98%)	0 (0%)	<0.001**
Vasopressor support		95 (93.1%)	0 (0%)	<0.001**

Statistically significant p values are written in bold. *: Man-Whitney U test was used. **: Chi-square test was used. SBP: Systolic Blood Pressure; IGC: Immature granulocyte count; IG%: Immature granulocyte percentage; WBC: white blood cell; NLR: Neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; RDW: Red blood cell distribution width; PDW: platelet distribution width; Hb: Hemoglobin; PLT: platelet; MPV: mean platelet volume; CRP: C-reactive protein; PCT: Procalcitonin; MV: mechanical ventilation.

Table 2. ROC analysis results of laboratory parameters according to in-hospital mortality.

Laboratory Parameters	AUC (95% CI)	p value	Cut-off level	Sensitivity	Specificity	NPV	PPV
IGC	0.74 (0.684-0.804)	<0.001	>0.035	76.5%	63.3%	85%	49.7%
IG%	0.86 (0.815-0.916)	<0.001	>0.45	75.5%	81.9%	87.6%	66.4%
NLR	0.70 (0.642-0.762)	<0.001	>6.65	78.4%	53%	83.8%	44.2%
RDW%	0.76 (0.709-0.821)	<0.001	>15.25	57.8%	82.8%	80.5%	61.5%
PDW	0.64 (0.573-0.707)	<0.001	>16.05	77.5%	45.8%	81%	40.5%
Hb	0.66 (0.601-0.736)	<0.001	<10.95	44.1%	86.5%	76.5%	60.8%
PLT	0.69 (0.621-0.758)	<0.001	<148	45.1%	91.6%	77.9%	71.9%
D Dimer	0.64 (0.575-0.707)	<0.001	>1550	38.2%	85.1%	74.4%	54.9%
CRP	0.83 (0.79-0.889)	<0.001	45,86	84.3%	72.1%	90.6%	58.9%
PCT	0.85 (0.806-0.894)	<0.001	>0.101	87.3%	69.8%	92%	57.8%
Albumin	0.86 (0.82-0.901)	<0.001	<38.3	83.3%	74.4%	90.4%	60.7%

ROC: Receiver operating characteristic, CI: Confidence interval; AUC: Area under the curve; NPV: Negative predictive value; PPV: Positive predictive value

Table 3. The multivariate logistic regression analysis of parameters in predicting in-hospital mortality.

Univariate				Multivariate			
Parameters	Odds rate	95% CI	p value	Parameters	Odds rate	95% CI	p value
IGC > 0.035	5.595	3.277-9.553	<0.001	IGC > 0.035	0.616	0.225-1.689	0.346
IG% > 0.45	13.899	7.868-24.556	<0.001	IG% > 0.45	4.387	1.727-11.145	0.002
NLR > 6.65	4.104	2.386-7.061	<0.001	NLR > 6.65	1.885	0.765-4.644	0.168
RDW% > 15.25	6.601	3.889-11.203	<0.001	RDW% > 15.25	3.628	1.414-9.309	0.007
PDW > 16.05	2.902	1.697-4.963	<0.001	PDW > 16.05	2.043	0.796-5.242	0.137
Hb < 10.95	5.064	2.912-8.803	<0.001	Hb < 10.95	1.804	0.727-4.479	0.203
PLT < 148	8.99	4.834-16.72	<0.001	PLT < 148	3.626	1.438-9.143	0.006
D Dimer > 1550	3.54	2.046-6.125	<0.001	D Dimer >1550	1.318	0.528-3.288	0.554
CRP > 45.86	13.885	7.536-25.586	<0.001	CRP > 45.86	2.356	0.964-5.755	0.06
PCT > 0.85	15.799	8.242-30.283	<0.001	PCT > 0.85	6.241	2.598-14.997	<0.001
Albumin <38.3	14.545	7.95-26.614	<0.001	Albumin < 38.3	3.998	1.63-9.807	0.002

The p value of the Hosmer-Lemeshow test was 0.441.

and laboratory findings of the surviving and non-surviving patient groups. When surviving and non-surviving patients were compared in terms of age and gender, 56 (54.9%) non-survivors were male, and no significant difference was detected in terms of both gender and age (p= 0.013, p= 0.281). Pulse, IGC, IG%, WBC, neutrophil, NLR, RDW, PDW, D-dimer, CRP, PCT levels, hospital stay, and the proportion of patients who needed MV and vasopressor drug support were significantly higher in the non-survivor group (p< 0.05 for all). Likewise, oxygen saturation, systolic blood pressure, lymphocyte, monocytes, Hb, PLT and albumin levels were found to be lower in the non-survivor group (p<0.05 for all).

The ROC analysis for predicting mortality of IGC, IG%, NLR, RDW%, PDW, Hb, PLT, D-dimer, CRP, PCT and albumin levels is shown in Table 2. Accordingly, compared to other parameters, IG% had the highest and PDW and D-dimer had the lowest AUC values (0.86, 0.64, 0.64, respectively) (p<0.001 for all). Furthermore, while the IG% cut-off value was >0.45, sensitivity was 75.5%, specificity was 81.9% , NPV reached 87.6% and PPV reached 66.4%.

When IGC and IG% levels were compared in patients who received and did not receive MV and vasopressor support, it was determined that IGC and IG% levels were significantly higher in those who received MV and vasopressor support (p<0.001 for all). The IG% was 1.1 (0.43-2.2) and 1.1 (0.4-2.2) in patients who received MV and vasopressor support, respectively, while it was 0.1 (0.005-0.3) and 0.1 (0.01-0.4) in those who did not. The IGC was 0.11 (0.04-0.32) and 0.11 (0.04-0.32) in patients who received MV and vasopressor support, respectively, while it was 0.03 (0.01-0.07) and 0.03 (0.01-0.07) in those who did not. Furthermore, the IG% of patients with a hospital stay longer

than 10 days was found to be significantly higher than that of those with a hospital stay of less than 10 days [respectively 0.5 (0.1-1.38), 0.2 (0.01-0.4), p<0.001].

According to logistic regression analysis, IG%, RDW%, PLT, CRP, PCT, and albumin levels were found to be independent markers of in-hospital mortality (Table 3).

Discussion

Cytokine storm is thought to have an important role in the worsening process of COVID-19. It is an uncontrollable, fatal and systemic inflammatory response that results in the release of large amounts of proinflammatory cytokines and chemokines [8]. Despite the fact that COVID-19 is a fatal disease, there is no fully accepted marker for predicting unfavorable results. Various markers of systemic inflammation have become available as part of expanded CBC in recent years. Since these biomarkers are simple and low cost, they can be easily used by clinicians in practice. In addition, according to current COVID-19 studies, hematological parameters have the property of being useful and valuable prognostic markers [2,3].

Studies have shown that IG levels, which can be easily and quickly measured by routine CBC, increase significantly in sepsis, infection and inflammation [9,10]. The presence of IGs in the peripheral circulation indicates greatly increased bone marrow activation and inflammation secondary to infection [4,11]. In a study of patients with severe COVID-19, both neutrophils and monocytes were shown to be predominantly of the immature phenotype [12]. In another CBC immunophenotyping study, it was emphasized that the increase in the number of immature neutrophils was strongly associated with disease severity and high IL-6 and IL-10 levels [13]. Selvi F et al. stated that IGC levels can be used to predict patients with COVID-19 (cut-off 0.03, while 66.7% sensitivity, 72.3% specificity and AUC: 0.718, p < 0.001) [14]. Alnor A et al. showed that IG levels in patients with severe COVID-19 increase as a disease-specific reaction and are associated with the severity of the disease [15]. Pozdnyakova O et al. found that the IGC values of patients with COVID-19 who were followed up in the intensive care unit (ICU) were significantly higher than those who were not followed up in the ICU (2.46 vs. 0.64, p = 0.02) [16]. Georgakopoulou V.E et al. also stated that the level of IGC in patients with COVID 19 is related to hospital stay length and disease severity (p=0.029, p=0.001). In addition, the authors showed that IG is an independent marker of intubation and mortality according to logistic regression analysis (OR, 13.98; p= 0.003 and OR, 42.17; p= 0.001) [6]. In our study, the IG levels in the patient group who did not survive were found to be significantly higher than in those who survived. In addition, patients with a hospital stay longer than 10 days had a significantly higher IG% than those with less than 10 days (p<0.001). Therefore, it can be thought that the IG level at admission is a marker related to the length of hospital stay and disease severity.

While most COVID-19 infections progress with mild symptoms, pneumonia that develops in some patients causes the activation of alveolar macrophages and lung epithelial cells by releasing proinflammatory cytokines. These cytokines may cause hyperinflammation and even the development of acute respiratory distress syndrome (ARDS) by stimulating the bone marrow to produce and release IGs [17,18]. Huang Y et al. predicted that high IG levels could detect high-risk patients for ARDS in the early period in patients with acute pancreatitis [19]. Birben B et al. stated that the Delta neutrophil index (DNI), which reflects the fraction of IG numbers, was significantly higher in the patient group who died from COVID-19, and that the relationship between mortality and DNI may be due to ARDS [20]. Alay GH et al. found a significant positive correlation between IG levels at presentation and mortality and intubation in patients with ARDS caused by COVID-19 (p = 0.001, r = 0.347 and p = 0.042, r = 0.102, respectively) [7]. In another study on COVID-19, it was stated that IG was associated with the degree of hypoxemia and an increase in IG values was detected in those who needed MV (OR = 16.41, p = 0.006) [21]. In our study, it was found that IG levels at admission were significantly higher in patients who received MV and vasopressor support compared to those who did not receive support (p<0.001). In addition, according to the ROC analysis, the IG% cut-off value was >0.45, with an AUC of 0.86, with a high predictive power for mortality (75.5% sensitivity, 81.9% specificity, 87.6% NPV). According to these results, IG levels at admission can be used as a marker to predict adverse outcomes and mortality in patients with severe COVID-19.

Despite the use of other accessible indicators, such as CRP, in the diagnosis of infectious illnesses, regular CBC analysis may determine IG levels rapidly and correctly at no extra expense [9]. In addition, IGs with a shorter half-life may reflect inflammation faster than those with a longer half-life [22]. In many studies, IG levels were compared with other blood parameters to evaluate the severity and prognostic power of the infection [14,23]. In a study of patients with acute appendicitis (AA), the ability of IGC to recognize AA early was found to be higher than other parameters (WBC, NLR, CRP) (AUC: 0.784, 98.3% sensitivity, 80% specificity) [24]. Van der Geest PJ et al. stated that IG% can replace CRP even when used alone in the estimation of infection in patients followed up in the ICU [4]. Myari A et al. emphasized that IG levels are higher in patients with critical COVID-19 (p<0.0001) and may be a useful indicator for these patients as well as NLR, WBC, and neutrophil levels (AUC: 0.890, sensitivity: 86%, specificity: 83%: cut-off >0.05) [3]. In the study by Alay GH et al., IG level at admission reached the highest predictive power of mortality compared to CRP, PCT and Ferritin according to logistic regression analysis (p= 0.026) [7]. Consistent with the literature, in our study, according to the results of logistic regression analysis, it was shown that IG% at admission had a higher predictive value compared to other parameters (OR: 4.387, p=0.002).

Limitation

First, this study was conducted retrospectively in a single center with a relatively limited number of patients. Since selection bias may occur in a retrospective study, multicenter and prospective studies are required to confirm the results of our study. Second, we were unable to determine the period between the beginning of symptoms and admission to the emergency room. This time span might have influenced the levels of IG and other inflammatory markers. Third, since serial IG measurements were only obtained during emergency stay, we cannot comment on changes in IG following therapy and their influence on

prognosis. Fourth, we could only examine short-term mortality in COVID-19 patients. As a result, we cannot anticipate IG's long-term clinical results.

Conclusion

According to our studies, IG levels upon admission are low-cost, easily accessible, and potent markers that may be used to predict mortality and prognosis in patients with severe COVID-19.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Foy BH, Carlson JCT, Reinertsen E, Padros I Valls R, Pallares Lopez R, Palanques-Tost E, et al. Association of red blood cell distribution width with mortality risk in hospitalized adults with SARS-CoV-2 infection. JAMA Netw Open. 2020;3(9):e2022058.

2. Kazancioglu S, Bastug A, Ozbay BO, Kemirtlek N, Bodur H. The role of haematological parameters in patients with COVID-19 and influenza virus infection. Epidemiol Infect. 2020;148:e272.

3. Myari A, Papapetrou E, Tsaousi C. Diagnostic value of white blood cell parameters for COVID-19:Is there a role for HFLC and IG. Int J Lab Hematol. 2022;44(1):104-11.

4. van der Geest PJ, Mohseni M, Brouwer R, van der Hoven B, Steyerberg EW, Groeneveld AB. Immature granulocytes predict microbial infection and its adverse sequelae in the intensive care unit. J Crit Care. 2014;29(4):523–7.

5. Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. Clin Infect Dis. 2021;73(11):4208-13.

6. Georgakopoulou VE, Makrodimitri S, Triantafyllou M, Samara S, Voutsinas PM, Anastasopoulou A, et al. Immature granulocytes: Innovative biomarker for SARS-CoV-2 infection. Mol Med Rep. 2022;26(1):217.

7. Alay GH, Tatlisuluoglu D, Bulut K, Fikri BI, Oztas A, Turan G. The Relationship between Immature Granulocyte Count and Mortality in ARDS Due to COVID-19. Niger J Clin Pract. 2022;25(8):1301-7.

8. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the `Cytokine Storm' in COVID-19. J Infect. 2020;80(6):607-13.

9. Nigro KG, O'Riordan M, Molloy EJ, Walsh MC, Sandhaus LM. Performance of an automated immature granulocyte count as a predictor of neonatal sepsis. Am J Clin Pathol. 2005;123(4):618–24.

10. Ünal Y, Barlas AM. Role of increased immature granulocyte percentage in the early prediction of acute necrotizing pancreatitis. Ulus Travma Acil Cerrahi Derg. 2019;25(2):177-82.

11. Mare TA, Treacher DF, Shankar-Hari M, Beale R, Lewis SM, Chambers DJ, et al. The diagnostic and prognostic significance of monitoring blood levels of immature neutrophils in patients with systemic inflammation. Crit Care. 2015;19(1):57.

12. Schulte-Schrepping J, Reusch N, Paclik D, Baßler K, Schlickeiser S, Zhang B, et al. Deutsche COVID-19 OMICS Initiative (DeCOI). Severe COVID-19 ıs marked by a dysregulated myeloid cell compartment. Cell. 2020;182(6):1419-40.e23.

13. Carissimo G, Xu W, Kwok I, Abdad MY, Chan YH, Fong SW, et al. Whole blood immunophenotyping uncovers immature neutrophil-to-VD2 T-cell ratio as an early marker for severe COVID-19. Nat Commun. 2020;11(1):5243.

14. Selvi F, Bedel C, Korkut M. Can the immature granulocyte count have a role in the diagnosis of coronavirus 2019 disease? Ibnosina J Med Biomed Sci. 2021;13:136-41.

15. Alnor A, Sandberg MB, Toftanes BE, Vinholt PJ. Platelet parameters and leukocyte morphology is altered in COVID-19 patients compared to non-COVID-19 patients with similar symptomatology. Scand J Clin Lab Invest. 2021;81(3):213-17.

16. Pozdnyakova O, Connell NT, Battinelli EM, Connors JM, Fell G, Kim AS. Clinical significance of CBC and WBC morphology in the diagnosis and clinical course of COVID-19 infection. Am J Clin Pathol. 2021;155(3):364-75.

17. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, Akinosoglou K, Antoniadou A, Antonakos N, et al. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. Cell Host Microbe. 2020;27(6):992-1000.e3.

18. Polidoro RB, Hagan RS, de Santis Santiago R, Schmidt NW. Overview: systemic inflammatory response derived from lung injury caused by SARS-CoV-2 infection explains severe outcomes in COVID-19. Front Immunol. 2020;11:1626.

19. Huang Y, Xiao J, Cai T, Yang L, Shi F, Wang Y, et al. Immature granulocytes: A novel biomarker of acute respiratory distress syndrome in patients with acute pancreatitis. J Crit Care. 2019;50:303-8.

20. Birben B, Birben OD, Akın T, Akkurt G, Surel AA, Yakısık E, et al. Efficacy of the delta neutrophil index in predicting 30-day mortality in COVID-19 patients requiring intensive care. Int J Clin Pract. 2021;75(5):e13970.

21. Dennison D, Al Khabori M, Al Mamari S, Aurelio A, Al Hinai H, Al Maamari K, et al. Circulating activated neutrophils in COVID-19: An independent predictor for mechanical ventilation and death. Int J Infect Dis. 2021;106:155-9.

22. Nahm CH, Choi JW, Lee J. Delta neutrophil index in automated immature granulocyte counts for assessing disease severity of patients with sepsis. Ann Clin Lab Sci. 2008;38(3):241-6.

23. Incir S, Calti HK, Palaoglu KE. The role of immature granulocytes and inflammatory hemogram indices in the inflammation. Int J Med Biochem. 2020;3(3):125-30

24. Korkut M, Bedel C, Selvi F. Are immature granulocytes and derivatives early predictors of acute appendicitis and acute complicated appendicitis in adults? Formos J Surg. 2020;53(4):123-7.

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